UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/532,547	08/24/2006	Gregory D. Plowman	EX03-075C-US	6196

63572 7590 12/23/2008

MCDONNELL BOEHNEN HULBERT @ BERGHOFF LLP
300 SOUTH WACKER DRIVE
SUITE 3100
CHICAGO, IL 60606

EXAMINER	
CANELLA, KAREN A	

ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
12/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/532,547	PLOWMAN ET AL.	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5 and 26-32* is/are rejected.

7)☒ Claim(s) *4 and 6-25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/8/05 12/18/06 9/19/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgement is made of applicant's election of the species of MAPK4. Applicant argues that the amended claim 1 now has unity of invention and therefore the Requirement for Species Election is improper. This has been considered but not found persuasive. Amended claim 1 and original claim 31 are not free of the art as evidenced by the rejections below. Thus, the instant claims lack a special technical feature over the prior art and Unity of Invention is lacking. The election of species requirement is deemed proper and adhered to. Claims 1 and 26 have been amended. Claims 1-32 are pending and examined on the merits to the extent that they read on MAPK4.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/420,554, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Acknowledgement is made of applicants claim to provisional applications 60/436,941, filed December 30, 2002 and 60/420,554, filed October 23, 2002. Upon review of said applications, it was noted that the '554 application discloses only two MBM proteins, that of CDC7L1 and PRKACG. The remainder of the instant MBM proteins are disclosed in the '941 application. Thus, the '554 application does not support the genus of MBM polypeptides encompassed by the instant claims 1-30. The '554 application also fails to adequately describe a genus of MBM proteins encompassed by claim31 as well. Accordingly

the instant claims are extended benefit of an earlier effective filing date only to December30, 2002.

Claim Objections

Claims 1-32 are objected to for reciting non-elected species.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2 and 28 are rendered vague and indefinite by the recitation of "small" molecule modulator. The term "small" in claims 2 and 28 is a relative term which renders the claim indefinite. The term "small" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Section 2173 of the M.P.E.P. states

Claims Must Particularly Point Out and Distinctly Claim the Invention

The primary purpose of this requirement of definiteness of claim language is to ensure that the scope of the claims is clear so the public is informed of the boundaries of what constitutes infringement of the patent..

In the instant case, the specification does not provide a limiting definition for a "small" molecule modulator which would provide a boundary between that which is "small" versus that which is not small, or "medium". Thus, a potential infringer would not be able to ascertain when a molecule was large enough not to be considered small, and therefore outside the scope of the claims..

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 28 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. .

Claim 28 is drawn o a method comprising contacting a mammalian cell with a agent that specifically binds a MAPK4 polypeptide or nucleic acid, wherein the agent is a small molecule modulator. Thus, the claim encompasses a genus of small molecule modulators that bind to a MAPK4 polypeptide or nucleic acid. The specification fails to disclose any molecules that bind to a MAPK4 polypeptide or nucleic acids other than an antibody and antisense nucleic acids.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather

than what it is. Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

In the instant case, a contemplation of a small molecule modulator which binds to MAPK4 polypeptide or nucleic acid is commensurate with defining the genus by function, and fails to provide adequate written description for a product required by the instant method claim. One of skill in the art would reasonably conclude that applicant as not in possession of the method of claim 28 as it pertained to small molecule modulators.

Claims 26-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of modulating branching morphogenesis in a mammalian cell in vitro or ex vivo, wherein modulating agent is a nucleic acid modulator, does not reasonably provide enablement for a method of modulating branching morphogenesis wherein the modulator is a small molecule inhibitor which binds to MAPK4, or an antibody which binds to MAPK4 or a method of modulating branching morphogenesis in vivo. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims..

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the

relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claims 26 requires the modulation of branching morphogenesis comprising contacting a cell with an agent that specifically binds to MAPK4 protein or nucleic acid. Claim 26 specifies that the agent is an antibody. It is noted that MAP kinases are intracellular kinases which translocate between the cytoplasm and the nucleus (Oncogenes, 2nd Edition, 1995, G. Cooper, page 292, legend for Figure 17.8). Thus, without evidence in the specification that the instant MAPK4 is present on the cell surface, or has an epitope present on the cell surface, one of skill in the art would be subjected to undue experimentation in order to bind an antibody to the MAPK4 protein in a cell in order to modulate branching morphogenesis,

Claim 26 requires the modulation of branching morphogenesis comprising contacting a cell with an agent that specifically binds a MAPK4 nucleic acid. When given the broadest reasonable interpretation, the "cell" of claim 26 includes cells found in vivo, and the "contacting" encompasses the administration of an antisense nucleic acid to MAPK4. Anti-sense therapy also requires uptake of the administered polynucleotide by the target cells. It is noted that many anti-sense therapies which appear to be promising using transfection in vitro, fail to provide any therapeutic efficacy when administered in vivo. For instance, Tolcher et al (Clinical Cancer Research, 2002, Vol. 8, pp. 2530-2535) teach that the administration of the anti-sense oligonucleotides ISIS 3521 and 5132 did not possess clinically significant single agent anti-tumor activity in patients having hormone-refractory prostate cancer, although said oligonucleotides were active inhuman tumor models (page 2533, second column, first paragraph under the heading "Discussion"); Cripps et al (Clinical Cancer Research. 2002, 8, pp. 2188-2192) teach that the same oligonucleotides evoked no clinical response in patients having metastatic colorectal cancer. Cripps et al note that although the steady state plasma levels for both oligonucleotide were above the IC50 for inhibition of mRNA expression, these levels may not have been achieved in the target tissue. Cripps et al also contemplate that additional reasons for the lack of efficacy can be that the target RNA was not important for the particular malignancy or that other unknown intracellular event prevented the drugs from effectively inhibiting protein production (page 2191, column 1, bridging paragraph. The specification fails to address the effect of the anti-sense compound on tumor cell in vitro, therefore it would be a

burden placed upon applicant to first attempt to ascertain if the mRNA was important to the cancerous phenotype of the cell as questioned by Cripps et al (ibid). The specification fails to provide a dosage schedule, and the plasma level of the administered oligonucleotides which would be commensurate with the appropriate dosage level at the target tissue, nor does the specification address a specific means for attaining the appropriate level within the target tissue that would result in the inhibition of the growth and proliferation of the cancer cells. Because of these deficiencies, one of skill in the art would be subject to undue experimentation without reasonable expectation of success in order to practice the claimed invention.

Claim 28 also includes the contacting of a cell with a small molecule modulator of MAPK4. The specification fails to teach such modulators. Although a modulator can be identified through a cell free assay such as that of claim 1, it would be necessary to determine such a genus of small molecule modulators before carrying out the instant invention which requires the structure of a small molecule modulator of MAPK4. It is noted that a method of screening or identifying such a molecule is not commensurate with teachings of how to make the modulator, and thus, a method of screening for such a small molecule modulator does not meet the requirements of 35 U.S.C. 112, first paragraph for how to make and use said modulator in a further invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Peng et al (Journal of Neurochemistry, 1996, Vol. 66, pp. 1191-1197).

Claim 1 is drawn in part to a method comprising the steps of providing an assay system comprising n MBM polypeptide or nucleic acid, contacting the assay system with a test agent under conditions whereby but for the presence of the test agent the system provides a reference activity and detecting a test-agent biased activity of the assay system, wherein a difference

between the test-agent-biased activity and the reference activity identifies the test agent as a candidate branching morphogenesis modulating agent, and wherein the MBM polypeptide s MAPK4.

Peng et al disclose a method of modulating the activity of MAPK4 using as assay system comprising MAPK4 (ERK4), wherein the modulator is nerve growth factor (page 1192, first column, lines 8-14) or EGF (page 1193, second column, under the heading "EGF as well ass NGF promotes tyrosine phosphorylation of ERK4"). Thus, the test-agent biased activity is tyrosine phosphorylation in response to the nerve growth factor.

It is noted that the recitation of a "method for identifying a candidate branching morphogenesis modulating agent" has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See In re Hirao, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and Kropa v. Robie, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

It is further noted that the phrase "herein a difference between the test agent-biased activity and the reference activity identifies the test agent as a candidate branching morphogenesis modulating agent" is not given patentable weight when comparing the claims to the prior art as it simply expresses the intended result of a process step positively recited, see MPEP 2111.04.

Given that the method of the prior art comprises the same method steps as claimed in the instant invention, the claimed method is anticipated because the method will inherently be a method for identifying a candidate branching morphogenesis modulating agent See Ex parte Novitski 26 USPQ 1389 (BPAI 1993).

Claims 1 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Petersen et al (Cell, 2000, vol. 103, pp. 1111-1120).

Claim 5 embodies the method of claim 1 wherein the assay system includes an expression assay comprising a MBM nucleic acid and the candidate test agent is a nucleic acid modulator.

Petersen et al disclose an assay wherein MAPK4 in Arabidopsis is transposon inactivated, and the resulting transposon tagged mutant was subjected to a RNA blot and cDNA microarray hybridization (page 1112, first column, second full paragraph, and Figure 1 C for the expression assay comprising the MBM nucleic acid (visible under the wild-type).

Given that the method of the prior art comprises the same method steps as claimed in the instant invention, the claimed method is anticipated because the method will inherently be a method for identifying a candidate branching morphogenesis modulating agent See Ex parte Novitski 26 USPQ 1389 (BPAI 1993)

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Takeishi et al (Journal of Molecular Cell Biology, 2001, Vol.33, pp. 1637-1648) as evidenced by Gonzales et al (FEBS Lett, 1992, Vol. 304, pp. 170-178).

Claim 2 embodies the method of claim1 wherein the candidate agent is a small molecule modulator. Claim 3 embodies the method of claim 2 wherein the screening assay is a kinase assay.

Takeishi et al disclose an in vitro kinase assay (page 1546, figure 7B and 7D) wherein isolate hart muscle exposed to chelerythrine or not exposed to chelerthrine, is subjected to mechanical stretching. The exposure to chelerythrine fulfills the specific embodiment of a small molecule modulator. Gonzales et al disclose that p63MAPK (which is synonymous with MAPK4) is expressed in heart muscle (page 177, Figure 5C). Thu, the assay system of Takeishi et al includes MAPK4.

Given that the method of the prior art comprises the same method steps as claimed in the instant invention, the claimed method is anticipated because the method will inherently be a method for identifying a candidate branching morphogenesis modulating agent See Ex parte Novitski 26 USPQ 1389 (BPAI 1993)

Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Lee et al (Molecular and Cellular Biology, 1999, Vol. 19, pp. 1973-1980), as evidenced by Gonzales et al (FEBS Lett, 1992, Vol. 304, pp. 170-178)..

Lee et al disclose an assay system comprising contacting H661 cells, which are a non-small cell lung cancer cells (page 1974, under the heading of Cell lines and culture conditions) with retinoic acid and serum and measuring GST-Jun, phosphorylated Jun, JNK and cJUN as a test-agent biased activity (page 1975, Figure 1). Retinoid acid fulfills the specific embodiments of a small molecule modulator. Gonzales et al disclose that p63MAPK (which is synonymous with MAPK4) is expressed in lung tissue (page 177, Figure 5C). Thus, the assay system of Lee et al includes MAPK4.

Given that the method of the prior art comprises the same method steps as claimed in the instant invention, the claimed method is anticipated because the method will inherently be a method for identifying a candidate branching morphogenesis modulating agent See Ex parte Novitski 26 USPQ 1389 (BPAI 1993)

Claims 31 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by the abstract of Whelan et al (Molecular Biology of the Cell, 2000, Vol. 11, supplement, page 456a).

Claims 31 and 32 are drawn to a method comprising obtaining a biological sample from a patient, contacting the sample with a probe for MBM expression, comparing the results to a control.

The abstract of Whelan discloses a method wherein western Blot was used to determine the level of ERK-4 (MAPK4) in primary breast tissue which meets the limitations of obtaining a biological sample from a patient and contacting the sample with a probe for BM expression because the labeled band in the Western blot would be indicative of a probe for MAPK4. The abstract of Whelan et al fulfills the embodiment of comparing the results with a control because the results were compared with the level of ERK-4 expression in adjacent breast tissue.

It is noted that the recitation of a "method for diagnosing a disease in a patient" has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See In re Hirao, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and Kropa v. Robie, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

It is further noted that the phrases "comparing results from step (b) with a control" and "determining whether step (c) indicates a likelihood of disease" are not given patentable weigh as said phrase indicate only abstract though rather than an active method step.

Given that the method of the prior art comprises the same method steps as claimed in the instant invention, the claimed method is anticipated because the method will inherently be a method for diagnosing disease in a patient, or diagnosing cancer in a patient See Ex parte Novitski 26 USPQ 1389 (BPAI 1993).

Claims 1-3, 5, 26-31 are rejected. Claims 4, 6-25 are objected to.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karen A Canella/
Primary Examiner, Art Unit 1643